Abstracts

Oral 17
Biomarkers

O17.1 THE DOSE-RESPONSE RELATION BETWEEN BENZENE AND PERIPHERAL BLOOD CELL COUNTS

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Introduction: Benzene is known to have toxic effects on the blood and bone marrow, but its impact at levels below the US occupational standard of 1 ppm remains uncertain. Furthermore, it has been hypothesised based on metabolic observations that benzene may have non-linear health effects.
Methods: We carried out a molecular epidemiology study of 250 exposed subjects and 140 unexposed subjects to evaluate haematologic, cytogenetic, and molecular endpoints in workers exposed to benzene, with a particular focus on exposures below 10 ppm. The study comprised a comprehensive exposure survey in which over a period of 16 months, 2783 personal air samples and 113 dermal measurements were collected complemented with urinary measurements of benzene and its metabolites and protein adducts of benzene oxide (BO) and 1,4-benzoquinone (1,4-BQ).
Results: The detailed exposure assessment enabled estimation of time specific individual exposure levels. In the last month before phlebotomy the median individual exposure of all 250 exposed workers was 1.2 ppm (10th–90th percentiles: 0.3–13.8 ppm) with 109 subjects exposed to less than 1 ppm. Exposure to other solvents except toluene was minimal and did not correlate with benzene exposure. We have previously reported that granulocyte, lymphocyte, B-cell, and platelet counts decreased with increasing benzene exposure and were significantly decreased in workers exposed to under 1 ppm benzene versus unexposed controls (Lan *et al*, *Science*, 2004). We are currently extending the work by evaluating the exact shape of the dose-response curve. Preliminary analyses indicate departure from linearity, possibly consistent with previous observations on BO and 1,4-BQ adduct formation.
Conclusion: Our analyses suggest that health effects related to benzene exposure may be non-linear.

O17.2 BIOLOGICAL MONITORING OF BENZENE EXPOSURE DURING TANK WORK ON AN OIL PRODUCTION SHIP ON THE NORWEGIAN CONTINENTAL SHELF

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Introduction: Benzene is a natural component of crude oil. During ordinary activity on oil production ships the workers' benzene exposure is low since most processes take place in closed systems. However, workers who maintain cargo tanks can be significantly exposed to benzene. The aim of this study was to assess the exposure to benzene during tank work by personal air sampling and by biological monitoring.
Methods: The study group (n = 13) included maintenance workers involved in cleaning, scaffold building, inspection, and welding in cargo tanks which contained residues of crude oil. The control group comprised employees in catering (n = 9). Personal exposure to benzene was measured by passive dosimeter badges (3M 3500). Biological samples (blood and urine) were collected *pre-shift*, *post-shift*, and *pre-next shift*. The level of unmetabolised benzene was measured in blood and urine, and the metabolites *t,t*-muconic acid and *S*-phenylmercapturic acid were measured in urine.
Results: Preliminary results show that when cleaning cargo tanks (n = 8) the geometric mean (GM) personal benzene exposure was 4.4 ppm (95% CI 2.0 to 9.7), while during inspection of the walls in a cleaned tank (n = 13) the GM exposure was 0.035 ppm (95% CI 0.023 to 0.052). Personal protective equipment was used during both tasks. After three consecutive work shifts the blood concentration was 17 nmol benzene/l (range 8–22 nmol/l) for maintenance workers who are analysed so far (n = 3 out of 13) compared with 0.6 nmol benzene/l (range 0.5–1 nmol/l) in the control group (n = 5 out of 9). The urine concentration was 46 nmol benzene/l (range 15–105 nmol/l) compared with 0.7 nmol benzene/l (range 0.5–2 nmol/l) in the control group. Final results will be presented.
Conclusion: More attention should be paid to the risk of benzene exposure during tank work. This is especially important for physically demanding tasks implying an increased uptake of hydrocarbons.

O17.3 PLASMA LEVEL OF PCB CONGENERS AND RISK OF MAJOR LYMPHOMA SUBTYPES

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Introduction: Results of lymphoma risk associated with PCB blood levels have been inconsistent thus far. We explored the hypothesis in a subset of cases and controls who participated in the European multicentre case control study on the aetiology of lymphoma (EPILYMPH).
Methods: We analysed seven PCB congeners regulated by the European Community, namely PCBs 28, 52, 101, 118, 138, 153, and 180, plus the congeners 170, and 194, in a plasma sample of 671 subjects (325 lymphoma cases and 338 controls) from four European countries participating to the EPILYMPH study. Risk of lymphoma overall and its major subtypes, according to the WHO classification, associated with increasing blood level of each individual PCB congener was calculated using unconditional logistic regression.
Results: When considering total PCB, we did not observe an association with lymphoma risk. Plasma PCB 28 levels above 79.9 ppb were associated with significantly elevated risks of lymphoma (all types) (OR = 2.4; 95% CI 1.4 to 4.1), diffuse large cell B lymphoma (DLCL) (OR = 3.8; 95% CI 1.7 to 8.5), and chronic lymphocytic leukaemia (CLL) (OR = 2.4; 95% CI 1.0 to 5.8). Trends in risk of lymphoma (all types), DLCL, and CLL were significant, and the risk increase was consistent by increasing quartile distribution of PCB28 plasma level. PCB 138 showed the strongest association in our study. Risk of lymphoma (all types) by quartiles was 1.0, 2.1 (95% CI 1.1 to 4.0), 2.9 (95% CI 1.6 to 5.5), 6.2 (95% CI 3.2 to 12.2), and 4.1 (95% CI 2.1 to 7.9), with a strongly significant upward trend. Risks were mostly elevated and upward trends statistically significant for DLCL and CLL, with 11–22 fold excess risks in the third and fourth quartile of PCB138 plasma level.
Conclusion: We showed an association between increased plasma levels of PCB28, and particularly PCB138, but not other PCB congeners, with an increasing risk of DLCL and CLL.

O17.4 IMPAIRED SPERM CHROMATIN INTEGRITY IN RELATION TO SERUM PCB-153 AND P,P′-DDE LEVELS IN EUROPEAN AND INUIT POPULATIONS

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Introduction: Polychlorinated biphenyls (PCBs), and dichlorodiphenyl dichloroethylene (p,p′-DDE), the major metabolite of dichlorodiphenyl trichloroethane (DDT), accumulate in the human body following occupational and environmental exposure. PCBs have weakly estrogenic or antiestrogenic activity in in vitro assays and p,p′.DDE exhibit antiandrogenic activity. Effects on male fertility is a concern but knowledge is very limited.

Methods: We examined cross sectional associations between lipid adjusted serum levels of organochlorines (PCB-153 and p,p′-DDE) and measures of human sperm chromatin integrity in four Inuit and European populations that were selected for a large epidemiological study to obtain high exposure contrasts to both compounds. The study included 707 adult males (193 Inuits from Greenland, 178 Swedish fishermen, 141 men from Warsaw, and 195 men from Kharkiv), who provided blood and semen samples in 2001–04 (participation rate <20% (fishermen) to 78% (Greenland)). The flow cytometric sperm chromatin structure assay (SCSA) was used to assess sperm chromatin integrity.
Results: The risk of impaired sperm chromatin integrity (DNA Fragmentation Index above the 75 percentile) increased with increasing level of PCB-153 among European men but not among Inuit men even the span of exposure levels was the largest in the latter group. No significant associations were found between SCSA derived parameters and p,p′-DDE serum concentrations.
Conclusion: The findings indicate that some organochlorines interfere with human semen quality but lack of consistency across all studied populations makes the evidence less strong unless the susceptibility to these compounds varies between different populations.

O17.5 NON-INVASIVE TEAR FILM BREAK UP TIME AND EYE BLINK TIME: BIOMARKER FOR EXPOSURE AND EFFECT IN INDOOR CLIMATE

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Introduction: Indoor exposure and effects were investigated in four brick University buildings in 2004, two with and two without suspected moisture damages. All were old blocks of flats built in ''Bergen cavity brick walls'' that had been reconstructed for University use. There were small differences in exposure assessments in respect of ventilation rates, thermal conditions, and air quality. All findings were within acceptable range. Assessment of tear film stability showed low values for workers in both types of buildings, compared to international literature. No significant differences were however found between the two groups. There was a need for an additional control group to further evaluate the tear film stability. The aim of this study was to get new data from a comparable population in another indoor environment.
Methods: A second control group were established in a 150 year old wooden building, which had been refurbished for use as University building. Tear film stability was studied by assessing tear film break up time by non-invasive ocular microscopy, based on a grid of equidistant circles of light that are blurred by tear film break up (NIBUT). ''Psychological BUT'' was acquired by recording the time the subject can keep the eyes open without pain, when watching a fixed point at the wall (self-reported BUT or PBUT).
Results: Forty two (85.7%) of 47 eligible employees in the wooden building participated. NIBUT and PBUT were compared with the aggregated brick building data from 2004 and showed marked and strongly significant differences ($p<0.005$, Student's *t* test two tailed). This suggests that both intervention and control groups in the study of 2004 might have been exposed to indoor environmental conditions that affects the eyes. NIBUT and PBUT in the wooden building were within the reported ''normal range'' values of NIBUT and PBUT.
Conclusion: The data show a reduced NIBUT and PBUT in brick buildings compared to a wooden building. These findings must be explored further, to find the explanation.